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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,113	03/15/2002	Juerg Lareida	000364.00124	8075

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,113	LAREIDA, JUERG	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5 and 7-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5 and 7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed July 14, 2004 have been received and entered into the application.

Action Summary

The rejection of claims 2,3 and 5 under 35 U.S.C. 112, first paragraph is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 2, 3 and 5-10 under 35 U.S.C. 102(e) as being anticipated by Graham (U.S.Patent No. 6,075,028) of record is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 2, 3, 5 and 9 under 35 U.S.C. 102(e) as being anticipated by Du Bois (U.S.Patent No. 6,399,601B1) is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 6-8 and 10 under 35 U.S.C. 103(a) as being unpatentable over Du Bois (U.S.Patent No. 6,399,601B1) in view of Gentile et al. (1984) second paragraph is hereby expressly withdrawn in view of Applicant's amendment.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2, 3, 5, 7, 8, 11 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Laties et al. (US 2002/0119974 A1).

Laties et al. teach method for the treating neuropathy including ischemic optic neuropathy (ischemic neuropathy) and macular degeneration (degenerative neuropathy) comprising administering sildenafil in the ranges from about 5 to about 250mg/day, more preferably from about 10 to 200mg/day, and most preferably from about 20 to about 150mg/day. (page 5, [0065], page 2 [0017] [0019], page 3 [0041] [0048]).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 3, 5, 7, 8 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Brewer et al. (1998) of record evidenced by Dorland's Illustrated Medical Dictionary (1994).

Brewer et al. teach sildenafil citrate therapy using 50 to 100mg given to patients with Parkinson's disease (autonomic degenerative neuropathy), diminution of parasympathetic nervous system function with impotence had positive results with minimal side effects. (title, background; results, conclusion).

Dorland's Illustrated Medical Dictionary teaches autonomic neuropathy is a functional disturbance or pathological condition involving the autonomic nervous system causing symptoms such as disorder of sexual functions. (page 1132).

Dorland's Illustrated Medical Dictionary is brought in to show that Parkinson's diseas is degenerative disease of autonomic neuropathy since Parkinson's disese like autonomic neuropathy resulted from a pathological condition causing symptoms such as disorder of sexual functions as taught by Brewer et al.

Claim Rejections - 35 USC § 103

Claims 2, 3, 5, 9, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Du Bois (U.S.Patent No. 6,399,601B1) of record in view of Ratsimamanga et al. (U.S.Patent No. 5,972,342) and further in view of Clary et al. (U.S.Patent No. 5,753,225).

Du Bois teaches a pharmaceutical composition comprising sildenafil for the treatment of diabetic complications such as neuropathy, nephropathy, and retinopathy. (abstract, column 23, line 63 through column 24, line 39, particularly, column 24, line 38). Du Bois teaches treatment of diabetic complication, such as neuropathy, nephropathy, retinopathy are included in the treatment of diabetes. (column 23, line 67 though column 24, line 2). Dubois teaches that sildenafil is a representative agent that can be used to treat diabetes. (column 24, lines 18-39).

Du Bois does not teach the specified amounts set forth in claim 5 and peripheral diabetic polyneuropathy set forth in claim 9 and a toxic neuropathy set forth in claim 12 and a metabolic neuropathy set forth in claim 13.

Ratsimamanga et al. teach diabetic neuropathy in its various forms including peripheral polyneuropathy and autonomous neuropathies. (column 9, lines 40-45).

Clary et al. teach etiologies of peripheral neuropathies and polyneuropathy include toxic agents and metabolic causes. (column 2, lines 37-47).

It would have been obvious to one of ordinary skill in the art to employ sildenafil comprising composition taught by Du Bois for the treatment of diabetic neuropathy in its various form including autonomous neuropathies and peripheral polyneuropathy and also treat the etiology of peripheral neuropathies including polyneuropathy (toxic neuropathies and metabolic neuropathies) because autonomous neuropathies and peripheral polyneuropathy are some of various forms of diabetic neuropathies and because Du Bois teaches that the composition comprising sildenafil is useful for the treatment of diabetic neuropathies which encompasses autonomous neuropathies and

peripheral polyneuropathy which is caused by toxic neuropathies and metabolic neuropathies as taught by Ratsimamanga et al. and Clary et al. respectively. To optimize the amount of sildenafil for the treatment of diabetic neuropathies is obvious since Du Bois teaches that sildenafil comprising composition is useful for the treatment of diabetic complications such as diabetic neuropathy encompassing various forms such as autonomous neuropathies and peripheral polyneuropathy. One would have been motivated to employ the composition comprising sildenafil taught by Du Bois for the treatment of any basic forms of diabetic neuropathy including autonomous neuropathies and peripheral polyneuropathy by administration of sildenafil in order to achieve effective treatment of diabetic neuropathy in general as taught by Du Bois et al.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Du Bois (U.S.Patent No. 6,399,601B1) as applied to claims 2,3,5,9, 12 and 13 above, and further in view of Gentile et al. (1984) of record.

Du Bois as applied as before and additional teachings as follows:

Du Bois teaches a pharmaceutical composition comprising sildenafil for the treatment of diabetic complications such as neuropathy, nephropathy, and retinopathy. (abstract, column 23, line 63 through column 24, line 39, particularly, column 24, line 38). Du Bois teaches treatment of diabetic complication, such as neuropathy, nephropathy, retinopathy are included in the treatment of diabetes. (column 23, line 67 though column 24, line 2). Dubois teaches that sildenafil is a representative agent that can be used to treat diabetes. (column 24, lines 18-39).

Du Bois does not teach gastroparesis or metabolic neuropathy set forth in claim 10.

Gentile et al. teach diabetic neuropathy of the alimentary canal takes several basic forms including gastroparesis.

It would have been obvious to one of ordinary skill in the art to employ sildenafil comprising composition taught by Du Bois for the treatment of diabetic neuropathy in its various form including gastroparesis (metabolic neuropathy) because Du Bois teaches that sildenafil comprising composition is useful for the treatment of diabetic complications such as diabetic neuropathy and because Gentile et al teach that gastroparesis is one of the form of diabetic neuropathy. One would have been motivated to employ the composition comprising sildenafil taught by Du Bois for the treatment of any basic forms of diabetic neuropathy including gastroparesis by administration of composition comprising sildenafil taught by Du Bois et al. with a reasonable expectation of successfully treating one of basic form of diabetic neuropathy, gastroparesis as generally taught by Du Bois et al.

For these reasons the claimed subject matter deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims allowed.

Response to Arguments

Applicant's arguments filed on July 14, 2004 have been fully considered but they are not persuasive. Applicant argues with respect to the rejection of the claims under 35 U.S.C. 103, the '601 patent (Dubois) is directed to compounds of formula I that differ substantially from sildenafil and are useful in the treatment of diabetes and in the treatment of diabetic complication and the patent goes on to state that a litany of other drugs having several different modes of action can be used in conjunction with the compounds of Formula I to treat diabetes. This is not persuasive because the cited patent (Dubois) encompasses the invention of the claims are drawn to. . . . .a method for a chemotherapeutic treatment... by application ... of a pharmaceutical agent "**comprising**" a compound of formula (I) (i.e. sildenafil) ... . Therefore, given the broadest interpretation of the claims of utilizing a pharmaceutical agent "comprising" a compound of formula (I) (i.e. sildenafil), the cited patent obviates the claimed subject matter since the cited patent clearly teaches the chemotherapeutic treatment comprising a pharmaceutical agent "comprising" including sildenafil. Applicant's next argues the '601 patent is absolutely silent with respect to an amount of sildenafil needed to treat diabetes, let alone an amount to treat an autonomous neuropathy. This is not persuasive because the amount of active agents to be utilized is within the knowledge of skilled artisan since the amount of the sildenafil require to treat autonomous neuropathy is well-known in the art as taught by Laties et al, and Brewer et al. Therefore, it would have been obvious to one of ordinary skill in the art to optimize the dosage of sildenafil to treat autonomous neuropathy well known in the art by Laties and

Brewer et al. for the specific neuropathy patients being treated. Applicant last argues the Gentile publication merely states that autonomic diabetic neuropathy of the alimentary canal takes several forms and that diabetics should be aware of bile disorders and it is totally silent with respect to using sildenafil to treat t neuropathy. This is not persuasive because Gentile et al. teaches gastroparesis is one of the forms of diabetic neuropathy therefore it would have been obvious to one of ordinary skill in the art the composition comprising sildenafil taught by Du Bois for the treatment of diabetic neuropathy encompasses its various forms including gastroparesis as taught by Gentile et al. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
November 2, 2004